

In vivo and in vitro immunogenicity of novel MHC class I presented epitopes for a therapeutic peptide-based vaccine against HTLV-1

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Background:

Human T-cell leukemia virus type 1 (HTLV-1) has infected approximately 20 million people worldwide. While 90% are asymptomatic, 5% develop severe diseases including adult T-cell leukemia/lymphoma (ATLL) and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). No vaccine against HTLV-1 exists, and screening programs are not universal. However, patients with chronic HTLV-1 infection have high frequencies of HTLV-1-activated CD8+ T cells, and the two main HLA alleles (A2, A24) are present in 88% of infected individuals.

Methods:

We utilized an immunoproteomics approach to characterize MHC-I restricted epitopes presented by HLA-A2+, A24+ MT-2 and SLB-1 cell lines. Unlike traditional motif prediction algorithms, this approach identifies epitopes associated with cytotoxic T-cell responses in their naturally processed forms, minimizing differences in antigen processing and protein expression levels.

Results:

Out of nine identified peptides, we confirmed six novel MHC-I restricted epitopes that were capable of binding HLA-A2 and HLA-A24 alleles and used in vitro and in vivo methods to generate CD8+ T cells specific for each of these peptides. MagPix MILLIPLEX data showed that in vitro generated epitope-specific CD8+ T cells secreted IFN- γ , granzyme B, MIP-1 α , TNF- α , perforin and IL-10 when cultured in the presence of MT-2 cell line. Degranulation assay confirmed cytotoxic response through surface expression of CD107 on CD8+ T cells when cultured with MT-2 cells. A CD8+ T-cell killing assay indicated significant antiviral activity of CD8+ T cells specific against all identified peptides. In vivo generated CD8+ T cells similarly demonstrated immunogenicity on ELISpot, CD107 degranulation assay, and MagPix MILLIPLEX analysis.

Conclusions:

These epitopes are thus candidates for a therapeutic peptide-based vaccine against HTLV-1, and our results provide preclinical data for the advancement of such a vaccine.

Disclosure of Interest Statement:

Nothing to disclose.

